

REMARKS

Claims 24-36 have been canceled without prejudice to expedite prosecution of this application. Applicant intends to pursue the broader aspects in a continuation application.

According to M.P.E.P. §2164.08:

The Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation'." In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Nevertheless, not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted. In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(Underlining added)

The sequence of SLIM3 was well-known and readily available to the skilled worker at the time the application was filed, and therefore it is unnecessary to incorporate it into the specification. For example, sequences for SLIM2 were disclosed in Morgan and Madgwick, BBRC, 225:632-338; Chan et al., Gene, 210:345-350, 1988 (Exhibit 1; SLIM2 is also known as FHL2 as stated on Page 347); and in various Genbank listings, including U60117 and Q14192 (Exhibit 2). Thus, withdrawal of the requirement to incorporate the sequence into the specification is respectfully requested.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

Appl. Serial No.: 09/428,647
Attorney Docket No.: SCH-1700
Reply Dated April 29, 2004

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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FILED: April 29, 2004

EXHIBIT

1

Molecular cloning and characterization of FHL2, a novel LIM domain protein preferentially expressed in human heart

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Received 25 April 1997; received in revised form 22 October 1997; accepted 23 October 1997; Received by A. Dugaiczky

Abstract

A full-length cDNA clone encoding a novel LIM-only protein was isolated and sequenced from a human fetal heart cDNA library. This full-length clone consists of 1416 base pairs and has a predicted open reading frame (ORF) encoding 279 amino acids. The ORF of this polypeptide codes for the human heart-specific four and a half LIM-only protein 2 (FHL2). It possesses an extra zinc finger that is a half LIM domain and four repeats of LIM domain. When the human FHL2 cDNA probe was used to hybridize with poly-A RNA of various human tissues, a very strong signal could be seen in heart tissues, and only moderately low signals could be detected in placenta, skeletal muscle and ovary. Virtually no signal could be detected in brain, lung, liver, kidney, pancreas, spleen, thymus, prostate, testis, small intestine, colon or peripheral blood leukocyte. FHL2 was mapped to chromosome 2q12–q13 by fluorescent in-situ hybridization (FISH). © 1998 Elsevier Science B.V.

Keywords: Heart cDNA; LIM domain protein; Zinc finger protein; Chromosome 2

1. Introduction

Zinc finger proteins can be classified based on different classes of consensus sequences. One class of zinc finger proteins bears a LIM motif that consists of a C₂HC motif and a C₄ motif (Liebhaber et al., 1990). LIM proteins are involved in cell identity, differentiation, and growth control (Dawid et al., 1994; Sanchez-Garcia and Rabbitts, 1994). They can be classified into three subclasses: (1) LIM-homeodomain proteins; (2) LIM-functional domain proteins, for example LIM kinases; and (3) LIM-only proteins. Many muscle-specific LIM proteins have been identified (Arber et al., 1994; Morgan et al., 1995; Morgan and Madgwick, 1996b; Jain et al.,

1996), and one of them has been associated with a key role in muscle development (Arber et al., 1994; Arber et al., 1997). In order to study the relationship between the LIM proteins and the differentiation and growth regulation of the heart, we have cloned and characterized three human heart cDNAs that code for LIM-only proteins (Tsui et al., 1994, 1996; Fung et al., 1995, 1996). In this study, we report the cloning and sequencing of a full-length cDNA that codes for a novel heart-specific four and a half LIM-only protein 2 (FHL2). We report here the tissue distribution of FHL2 as revealed by Northern hybridization and the chromosomal mapping of the FHL2 gene by fluorescent in-situ hybridization (FISH). The possible roles of FHL2 are also discussed.

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Abbreviations: aa, amino acid(s); BLAST, Basic Local Alignment Search Tool; FHL2, four and a half LIM-only protein 2; FISH, fluorescent in-situ hybridization; MLP, muscle LIM protein; MRF, muscle regulatory factor; NCBI, National Center for Biotechnology Information; ORF, open reading frame; PCR, polymerase chain reaction; SLIM3, skeletal muscle LIM-protein 3.

2. Experimental and discussion

2.1. Isolation of the FHL2 cDNA

Partial sequencing of cDNA clones isolated from a directionally cloned human fetal heart (10–12 weeks)

1	C	AGA	AGG	TTG	GGG	CCA	TCC	AAC	CAG	GCA	GTC	CGC	CTG	CAC	AGC	AGC	46
47	TGT	CCC	TGC	TCA	TGC	GGC	TGG	AGG	ACA	GAA	GAC	AGA	ACC	CTA	AAA	CCA	94
1	CAG	GTT	GCT	GAA	AAA	CCA	GGA	GTC	AAA	ATG	ACT	GAG	CGC	TTT	GAC	TGC	7
95																	142
8	H	H	C	N	H	S	L	P	G	K	K	Y	I	L	R	E	23
143	CAC	CAT	TGC	AAC	GAA	TCT	CTC	TTT	GGC	AAG	AAG	TAC	ATC	CTG	CGG	GAG	190
24	E	S	P	Y	C	V	V	C	F	E	T	L	F	A	N	T	39
191	GAG	AGC	CCC	TAC	TGC	GTG	GTG	TGC	TTT	GAG	ACC	CTG	TTC	GCC	AAC	ACC	238
40	C	E	E	C	G	R	P	I	G	C	D	C	K	D	L	S	55
239	TGC	GAG	GAG	TGT	GGG	AAG	CCC	ATC	GGC	TGT	GAC	TGC	AAG	GAC	TTG	TCT	286
56	Y	E	D	R	H	W	H	E	A	C	F	H	C	S	O	C	71
287	TAC	AAG	GAC	CGG	CAC	TGG	CAT	GAA	GCC	TGT	TTC	CAC	TGC	TGC	CAG	TGC	334
72	R	N	S	L	V	D	K	P	F	A	A	K	E	D	O	L	87
335	AGA	AAC	TCA	CTG	GTG	GAC	AAG	CCC	TTT	GCT	GCC	AAG	GAG	GAC	CAG	CTG	382
88	L	C	T	D	C	Y	S	H	E	Y	S	S	K	C	Q	E	103
383	CTC	TGT	ACA	GAC	TGC	TAT	TCC	AAC	GAG	TAC	TCA	TCC	AAG	TGC	CAG	GAA	430
104	C	K	K	T	I	M	P	G	T	R	K	M	E	Y	K	G	119
431	TGC	AAG	AAG	ACC	ATC	ATG	CCA	GGT	ACC	CGC	AAG	ATG	GAG	TAC	AAG	GGC	478
120	S	S	W	H	E	T	C	F	I	C	H	R	C	Q	Q	P	135
479	AGC	AGC	TGG	CAT	GAG	AGC	CCC	TTC	ATC	TGC	CAC	CGC	TGC	CAG	CAG	CCA	526
136	I	G	T	K	S	F	I	P	K	D	N	O	N	F	C	V	151
527	ATT	GGA	ACC	AAG	AGT	TTC	ATC	CCC	AAA	GAC	AAT	CAG	AAT	TTT	GTT	GTC	574
152	P	C	Y	E	K	Q	H	A	M	Q	C	V	Q	C	K	H	167
575	CCC	TGC	TAT	GAG	AAA	CAA	CAT	GCC	ATG	CAG	TGC	GTT	CAG	TGC	AAA	ATG	622
168	P	I	T	T	G	G	V	T	Y	R	E	Q	P	W	H	K	183
623	CCC	ATC	ACC	ACG	GGA	GGG	GTC	ACT	TAC	CGG	GAG	CAG	CCC	TGG	CAC	AAG	670
184	E	C	F	V	C	T	A	C	R	K	Q	L	S	G	Q	R	199
671	GAG	TGC	TTC	GTG	TGC	ACC	GCC	TGC	AGG	AAG	CAG	CTG	TCT	GGG	CAG	CGC	718
200	F	T	A	R	D	D	F	A	Y	C	L	N	C	F	C	D	215
719	TTC	ACA	GCT	CGC	GAT	GAC	TTT	GCC	TAC	TGC	CTG	AAC	TGC	TTT	TGT	GAT	766
216	L	Y	A	K	K	C	A	G	C	T	N	P	I	S	G	L	231
767	TTG	TAT	GCC	AAG	AAG	TGT	GCT	GGG	TGC	ACC	AAC	CCC	ATC	AGC	GGA	CTT	814
232	G	G	T	K	Y	I	S	F	E	E	R	Q	W	H	N	D	247
815	GCT	GGC	ACA	AAA	TAC	ATC	TCC	TTT	GAG	GAA	CGC	CAG	TGC	CAT	AAC	GAC	862
248	C	F	N	C	K	K	C	S	L	S	L	V	G	R	G	F	263
863	TGC	TTT	AAC	TGT	AAG	AAG	TGC	TCC	CTC	TCA	CTG	GTG	GGG	CGT	GGC	TTC	910
264	L	T	E	R	D	I	L	C	P	D	C	G	K	D	I	E	279
911	CTC	ACA	GAG	AGG	GAC	GAC	ATC	CTG	TGC	CCC	GAC	TGT	GGG	AAA	GAC	ATC	958
280	*																280
959	TGA	ATT	CAA	CAC	AGA	GAA	GTT	GCT	GCT	TGT	GAT	CTC	ACA	CAC	AGA	TTT	1006
1007	TTA	TGT	TTT	CTT	TCT	CAC	CCA	GGC	AAT	CTT	GCC	TTT	TGC	TTT	CTT	CCA	1054
1055	GCC	ACA	TTG	AGA	CTT	TCT	TCT	AGT	GCT	TTT	CAG	TGA	TAC	TCA	CGT	TTG	1102
1103	CTT	AAA	CCC	TTT	AGT	GCT	TTG	TGA	TAG	TTC	AGT	CCC	AGG	GAA	AGA	GAA	1150
1151	AAC	TGC	CCC	TAG	GCC	CTA	GGT	GGG	AAG	ATG	GTT	TGA	AAT	TTT	TGT	AAT	1198
1199	CGA	GTA	AGG	CAC	ACC	CAA	ATG	TAA	AAA	TCC	TTT	TGA	ATG	ATG	CCT	TTA	1246
1247	TAA	ATC	TTT	CTC	TCA	CTG	TCT	ATT	TAA	GTG	CAA	TTA	ACA	TAT	GTG	ACA	1294
1295	AAC	TTG	AAA	GTT	TTC	TAA	ACT	CAA	TAA	GGT	AAT	GAC	CAG	TTG	TTA	TTT	1342
1343	ACA	GCT	CTG	TAA	CCT	CCC	GTT	GCG	TCA	AGT	CTA	AAC	CAA	GAT	TAT	GTG	1390
1391	ACT	TGC	<u>AAT</u>	<u>AAA</u>	GTT	ATT	CAG	AAC	AG								1416

Fig. 1. cDNA and predicted amino-acid sequences of FHL2. The nucleotide sequence data has been submitted to the GenBank/EMBL Data Libraries under the accession number U29332. In the DNA sequence, the polyadenylation signal (AATAAA) is underlined. **Methods:** Partial sequencing of cDNAs clones from a directionally cloned human fetal heart (10–12 weeks) library was conducted as described (Hwang et al., 1995; Liew et al., 1994; Tsui et al., 1995). Briefly, eluted phage plaques were subjected to PCR in the presence of primers flanking the restriction sites of the lambda gt22 vector (forward: 5'-ATTGGTGGCGACGACTCCTGGA-3'; reverse: 5'-TTTG-ACACCAGACCAACTGGTA-3'). PCR products were sequenced directly using a cycle sequencing kit (dsDNA Cycle Sequencing System, Life Technologies) in the presence of 160 nM of a fluorescein-conjugated primer nested within the forward PCR primer (fluorescein-5'-GGTGGCGACGACTCCTGGAGCC-3'). The sequencing products were run and analysed in a Pharmacia A.L.F. DNA sequencer. Sequence comparisons against the GenBank and EMBL nucleotide and protein databases were performed using the BLAST electronic mail server (Altschul et al., 1990). The complete sequence of the cDNA was determined by primer walking strategy using dideoxy sequencing.

cDNA library was conducted as described (Liew et al., 1994; Hwang et al., 1995; Tsui et al., 1995). Briefly, eluted phage plaques were subjected to polymerase chain reaction (PCR) in the presence of primers flanking the restriction sites of the lambda gt22 vector. PCR products were sequenced, and one of the cDNA clones exhibited a DNA sequence similarity to that of the LIM domain protein family. The putative protein encoded by this cDNA is named heart-specific four and a half LIM-only protein 2 (FHL2). The PCR product of FHL2 cDNA clone was subcloned into the plasmid pGBT9. The DNA sequence of the open reading frame of FHL2 was verified by sequencing with T7 DNA polymerase.

Excluding the vector sequence and the poly (A) region, the FHL2 cDNA insert is 1416 base pairs in length. The initiation and stop codons were found at nucleotide numbers 122 and 959, respectively. A typical polyadenylation signal (AATAAA) was found at nucleotide number 1397–1402 (Fig. 1).

2.2. Sequence analysis of FHL2

After translating the open reading frame (ORF) of the FHL2 cDNA clone, a protein sequence of 279 amino acids was obtained (predicted molecular weight = 32.1 kDa) (Fig. 1). The isoelectric point of the predicted protein is 7.2 as determined by the software PROSIS. The cDNA clone was named human heart-specific four and a half LIM-only protein 2 (FHL2). It possesses an extra zinc finger that is a half LIM domain and four repeats of LIM domain. LIM domains are predicted to bind two molecules of Zn^{2+} to form two zinc-finger-like structures (Michelsen et al., 1993). Therefore, one molecule of FHL2 could bind up to nine Zn^{2+} and form nine zinc fingers. This FHL2 is unique because it possesses an odd number of zinc fingers as compared with other LIM-only proteins. When the LIM domains of FHL2 and other LIM proteins are aligned, some notable features can be observed (Fig. 2). The consensus sequence of the four LIM domains is **CX₂CX₃IX₁₁₋₁₅WHX₂CFXCX₂CX₃(I/L)X₄(F/Y)X₈CX₂C** (C, cysteine; H, histidine; I, isoleucine; W, tryptophan; F, phenylalanine; L, leucine; Y, tyrosine; X, any amino residues. The conserved amino-acid residues are represented by bold letters). The hydrophobic residues (I/L) and (F/Y) are present in many zinc fingers that have

PCR of FHL2 cDNA clone was performed by using a pair of primers flanking the open reading frame (ORF) of FHL2 (forward: 5'-TAGGGCGAATTCATGACTGAGCGCTTTGACTGCCA-3'; reverse: 5'-AGGGCGTCCGACTCAGATGTCTTTCCACAGTCGG-3'). Both primers have an end clamp (TAGGGC) which facilitated cleavage by restriction enzymes. An *Eco*RI site and an *Sal*I site are present in the forward and reverse primers, respectively. After digestion with *Eco*RI and *Sal*I, the PCR fragment was subcloned into the plasmid pGBT9.

SLIM3 partial cDNA, which codes for only 153 amino-acid residues of the carboxyl terminal of FHL2 (Fig. 2). Another difference is that the SLIM3 sequence is incomplete at the 3' untranslated region. The second homologous sequence was an unpublished DNA sequence encoding a LIM protein called DRAL (Genini et al., 1996a). The DRAL clone was isolated from a human neonatal skeletal muscle cDNA library. There was 96.7% identity between the cDNA sequences of FHL2 and DRAL (data not shown). Although the coding regions of FHL2 and DRAL are similar, the 5' non-coding regions are very different from each other. When the amino-acid sequences of FHL2 and DRAL were aligned, a 99.6% identity between these two proteins was found (Fig. 2), with only a difference of one amino-acid residue. At position 167, methionine (M) in FHL2 was replaced by lysine (K) in DRAL. Previous studies have shown that DRAL cDNA is expressed in primary myoblasts but down-regulated in the embryonal-rhabdomyosarcoma (RMS) cell line RD (Genini et al., 1996b).

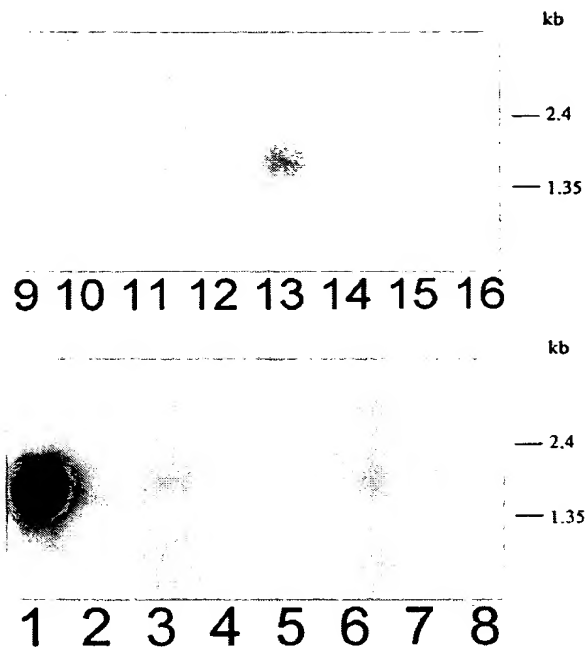


Fig. 3. Northern hybridization of FHL2 in human tissues. Key of the lanes: 1, heart; 2, brain; 3, placenta; 4, lung; 5, liver; 6, skeletal muscle; 7, kidney; 8, pancreas; 9, spleen; 10, thymus; 11, prostate; 12, testis; 13, ovary; 14, small intestine; 15, colon; 16, peripheral blood leukocyte. **Methods:** Two Northern blots containing poly-A RNA from a variety of human tissues were obtained from Clontech Laboratories. Radioactively labeled random primed probe was made by using the purified PCR product of FHL2 as the template. Blots were prehybridized for 6 h and hybridized at 42°C for 18–20 h. Membranes were then washed in $1 \times$ SSC twice and washed again in $0.1 \times$ SSC with 0.1% SDS at 42°C to remove non-specific annealing. Autoradiography was performed at -70°C for 48–72 h.

Therefore, we believe that FHL2 may play a crucial role in the development and differentiation of human muscles.

2.3. Tissue distribution of FHL2

When the human FHL2 cDNA probe was used to hybridize with poly (A) RNA of various human tissues, the tissue distribution of the FHL2 mRNA was revealed (Fig. 3). It was shown that a very strong signal could be seen in the heart tissue. Only moderately low signals could be detected in placenta, skeletal muscle and ovary. Virtually no signal could be detected in brain, lung, liver, kidney, pancreas, spleen, thymus, prostate, testis, small intestine, colon or peripheral blood leukocyte. These results show that FHL2 is a LIM-only protein that is preferentially expressed in heart. When the cDNA sequence of FHL2 was searched against the database of expressed sequence tags (dbEST), 17 partial sequences matched with FHL2, 12 originated from fetal heart, two from adult heart, one from ovary, one from fetal spleen and one from senescent fibroblasts. This result supports

our data showing that FHL2 is differentially expressed in heart. Previous results have shown that SLIM3 is expressed in human skeletal muscle (Morgan and Madgwick, 1996b). However, we have shown that heart has the highest level of FHL2 expression. Therefore, we suggest that FHL2 is a more appropriate name than SLIM3. Interestingly, MLP, which is a LIM-only protein with two LIM domains, is also highly expressed in the human heart. Its expression is enriched in striated muscle and occurs concomitantly with terminal muscle differentiation. Over-expression of MLP in C2C12 myoblasts promotes muscle differentiation, whereas antisense MLP prevent myogenesis (Arber et al., 1994). Similarly, MLP-deficient mice developed dilated cardiomyopathy with hypertrophy, heart failure and disruption of cardiomyocyte cytoarchitecture after birth (Arber et al., 1997). Since FHL2 has a high expression level in adult heart, we speculate that FHL2 may be particularly important for the maintenance of the heart phenotype. Besides, one of the LIM domains-LIM1 of MLP appears to play a role in nuclear localization, interacting with the muscle regulatory factors (MRFs) and enhancing the formation of MRF-DNA complexes, whereas another LIM domain-LIM2 primarily interacts with cytoplasmic proteins involved in maintaining the cellular architecture (Arber and Caroni, 1996; Kong et al., 1997). Thus, it might be possible that the LIM domains of FHL2 also function as specific adapter elements to promote the assembly and targeting of multiprotein complexes. Such speculation awaits further investigation in finding the protein partners of FHL2.

2.4. Chromosomal mapping of FHL2 gene

The FHL2 gene is located at chromosome 2q12–q13 (Fig. 4). No significant FISH signals were observed from other chromosomes. Also located in this region, according to the database of NCBI, are paired box homeotic gene 8 (Stapleton et al., 1993), engrailed homolog 1 (Kohler et al., 1993), interleukin 1 alpha (Lafage et al., 1989), interleukin 1 beta (Webb et al., 1986), interleukin 1 receptor alpha (Copeland et al., 1991), interleukin 1 receptor beta (McMahan et al., 1991), activin AB beta polypeptide (Barton et al., 1989), T-cell differentiation protein mal (Alonso et al., 1988), *v-ral* oncogene homolog B (Hsieh et al., 1990), 70-kDa tyrosine phosphoprotein (Ku et al., 1994), gibbon ape leukemia virus receptor 1 (Kaelbling et al., 1991), diazepam binding inhibitor (Mocchetti, 1990), nucleolin (Srivastava et al., 1990), protein C (Patracchini et al., 1989), lysosomal H^+ transporting ATPase (Ozcelik et al., 1991) and cytochrome c oxidase subunit Vb (Lomax et al., 1991). Moreover, familial juvenile nephronophthisis (Hildebrandt et al., 1995) and the pericentric inversion (Pallotta, 1991), *inv(2)(p12q14)*, which results in a syndrome of iris coloboma, bilateral

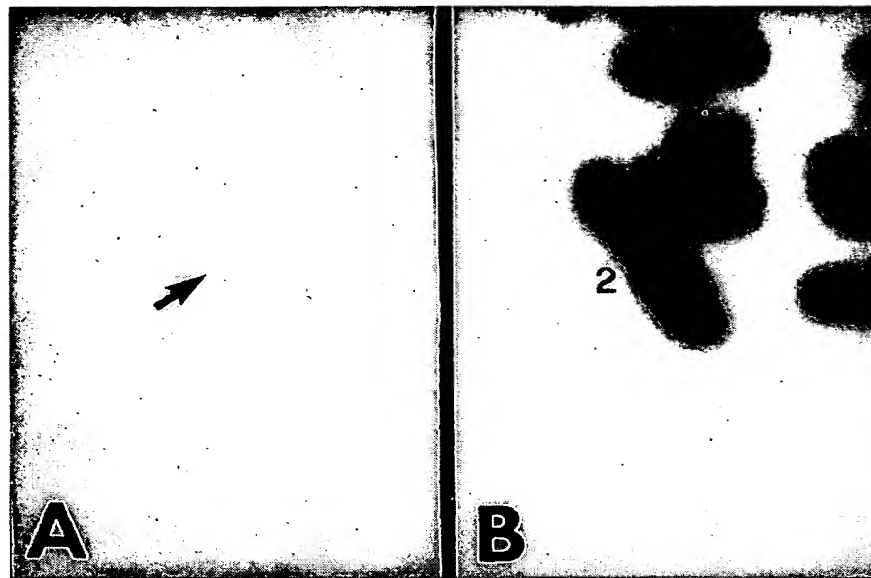


Fig. 4. FISH mapping. (A) FISH signals on chromosome. (B) Same mitotic figures stained with DAPI to identify chromosome 2. **Methods:** The chromosomal mapping of the FHL2 gene was performed by Dr H.H.Q. Heng of SeeDNA Biotech Inc. (Ontario, Canada). The pGBT9-FHL2 plasmid was biotinylated with dATP using the BRL BioNick labelling kit. The procedure for fluorescent in-situ hybridization (FISH) detection was performed essentially as described by Heng et al. (1992) and Heng and Tsui (1993).

oculotosis, hypertelorism, broad nasal bridge, and prominent epicanthic folds, have been mapped to this region. Recently, we have also mapped human FHL1 (alias: SLIM1), which has the same domain structure as FHL2, to chromosome X (manuscript in preparation). Therefore, although FHL2 and FHL1 belong to the same family of LIM proteins expressed in muscles (Morgan and Madgwick, 1996b), they are located at different regions of the human genome.

2.5. Conclusions

- (1) A human fetal heart cDNA (1416 bp) encoding a novel LIM-only protein was isolated and characterized.
- (2) The predicted ORF (encoding 279 aa) of this cDNA codes for the human heart-specific four and a half LIM-only protein 2 (FHL2). It possesses an extra zinc finger that is a half LIM domain and four repeats of LIM domain.
- (3) The FHL2 is preferentially expressed in heart, only moderately expressed in placenta, skeletal muscle and ovary and there is virtually no expression in brain, lung, liver, kidney, pancreas, spleen, thymus, prostate, testis, small intestine, colon or peripheral blood leukocyte.
- (4) The FHL2 was mapped to chromosome 2q12–q13 by FISH.

Acknowledgement

We would like to thank Dr Henry H.Q. Heng for mapping the FHL2 by FISH. This study was supported by earmarked grants from Research Grant Council, Hong Kong (Ref. No.: CUHK 418/95M and 205/96M) and the Ho Sin Hang Education Endowment Fund.

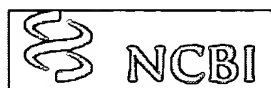
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EXHIBIT

2



Entrez

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Limits

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20

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File

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Featui

☐ 1: Q14192. Skeletal muscle L...[gi:2497681]

BLink, Domains, Links

LOCUS Q14192 279 aa linear PRI 15-DEC-1998

 DEFINITION SKELETAL MUSCLE LIM-PROTEIN 3 (SLIM 3) (LIM-DOMAIN PROTEIN DRAL)
 (FOUR AND A HALF LIM DOMAINS PROTEIN 2) (FHL-2).

ACCESSION Q14192

VERSION Q14192 GI:2497681

 DBSOURCE swissprot: locus SLI3_HUMAN, accession Q14192;
 class: standard.
 extra accessions: Q13229, Q13644, created: Nov 1, 1997.
 sequence updated: Nov 1, 1997.
 annotation updated: Dec 15, 1998.

 xrefs: gi: [1160931](#), gi: [1160932](#), gi: [1845201](#), gi: [1377897](#), gi:
[1381811](#), gi: [1381812](#)

 xrefs (non-sequence databases): MIM [602633](#), PFAMPF00412,
 PROSITEPS00478, PROSITEPS50023

KEYWORDS Repeat; LIM motif; Metal-binding; Zinc; Zinc-finger.

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens

 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Mammalia;
 Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (residues 1 to 279)

 AUTHORS Genini, M., Schwalbe, P., Scholl, F.A., Remppis, A., Mattei, M.G. and
 Schafer, B.W.

 TITLE Subtractive cloning and characterization of DRAL, a novel
 LIM-domain protein down-regulated in rhabdomyosarcoma

JOURNAL DNA Cell Biol. 16 (4), 433-442 (1997)

MEDLINE [97294674](#)

REMARK SEQUENCE FROM N.A.

TISSUE=SKELETAL MUSCLE

REFERENCE 2 (residues 1 to 279)

AUTHORS TSUI, S., LIM, N., FUNG, K., WAYE, M. and LEE, C.

TITLE Direct Submission

JOURNAL Submitted (~JUN-1996)

REMARK SEQUENCE FROM N.A.

TISSUE=HEART

REFERENCE 3 (residues 1 to 279)

AUTHORS Morgan, M.J. and Madgwick, A.J.

 TITLE Slim defines a novel family of LIM-proteins expressed in skeletal
 muscle

JOURNAL Biochem. Biophys. Res. Commun. 225 (2), 632-638 (1996)

MEDLINE [96354835](#)

REMARK SEQUENCE OF 127-279 FROM N.A.

TISSUE=HEART MUSCLE

COMMENT

 This SWISS-PROT entry is copyright. It is produced through a
 collaboration between the Swiss Institute of Bioinformatics and
 the EMBL outstation - the European Bioinformatics Institute.
 The original entry is available from <http://www.expasy.ch/sprot>
 and <http://www.ebi.ac.uk/sprot>

[TISSUE SPECIFICITY] EXPRESSED ONLY IN SKELETAL MUSCLE.
[SIMILARITY] CONTAINS 4 LIM DOMAINS. THE LIM DOMAIN BINDS 2 ZINC IONS.

FEATURES	Location/Qualifiers
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<u>gene</u>	1..279 /gene="FHL2" /note="synonyms: SLIM3, DRAL"
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<u>Region</u>	40..92 /gene="FHL2" /region_name="Domain" /note="LIM 1."
<u>Region</u>	101..153 /gene="FHL2" /region_name="Domain" /note="LIM 2."
<u>Region</u>	162..212 /gene="FHL2" /region_name="Domain" /note="LIM 3."
<u>Region</u>	167 /gene="FHL2" /region_name="Conflict" /note="M -> G (IN REF. 1)."
<u>Region</u>	221..275 /gene="FHL2" /region_name="Domain" /note="LIM 4."

ORIGIN

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121 swhetcfich rcqqpigtkf fipkdnqnfq vpcyekqham qcvqckmpit tggvtyreqp
181 whkecfvcta crkqlsgqrf tarddfaycl ncfcdlyakk cagctnpisg lggtkyisfe
241 erqwhndcfh ckkcslsivg rgflterddi lcpdcgkdi
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